Claims

1. An assay method which includes:

bringing into contact a putative modulator and a VDU1 polypeptide;

determining whether the putative modulator binds and/or modulates an activity of VDU1;

determining the effect of the putative modulator on HIF-α stability and/or on the ubiquitination state of HIF-α, in a test system comprising HIF-α and VDU1.

2. An assay method according to claim 1, which includes:

bringing into contact a VDU1 polypeptide with a putative modulator;

determining binding between the VDU1 polypeptide and the putative modulator;

bringing the putative modulator into contact with a test system comprising VDU1 and HIF-α; and

determining the effect of the putative modulator on the stability and/or state of ubiquitination of HIF-α.

3. An assay method according to claim 1 which includes:

bringing into contact a VHL polypeptide, a VDU1 polypeptide and a putative modulator;

determining whether the putative modulator modulates the interaction of the VHL and VDU1 polypeptides;

bringing the putative modulator into contact with a test system comprising VDU1, VHL and HIF-α;

determining the effect of the putative modulator on the stability and/or state of ubiquitination of HIF-α.

4. An assay method according to claim 3, wherein the assay method comprises bringing into contact a VHL polypeptide, a VDU1 polypeptide and a putative modulator compound under

conditions where the VHL polypeptide and the VDU1 polypeptide, in the absence of modulator, are capable of forming a complex.

5. An assay method which includes:

bringing a putative modulator into contact with VDU1 and an ubiquitinated VDU1 substrate;

determining the ability of the putative modulator to modulate the stabilisation and/or state of ubiquitination of the substrate by VDU1;

bringing the putative modulator into contact with a test system comprising VDU1 and HIF-α;

determining the effect of the putative modulator on the stability and/or state of ubiquitination of HIF-α.

6. An assay method according to any one of claims 1,2, or 5 in which the test system further comprises VHL.

7. An assay method according to any one of the preceding claims, wherein the test system is a cell.

8. An assay method according to claim 7, wherein the cell is under hypoxic conditions.

9. An assay method according to claim 7, wherein the cell is under normoxic conditions.

10. An assay method according to any one of claims 7 to 9, wherein the effect of the putative modulator on HIF-α stability is determined by the activity of a HIF-responsive reporter gene.

11. An assay method which includes:

bringing into contact a putative modulator with a test system comprising VDU1 and ubiquitinated HIF-α;

determining the ability of the putative modulator to modulate the stabilisation and/or state of ubiquitination of HIF-α by VDU1.

12. An assay method according to claim 11 in which the test system further comprises VHL.

13. An assay method according to any one of the preceding claims, wherein the putative modulator is brought into contact with the test system under conditions where VDU1 is capable of stabilising HIF-α, in the absence of the modulator.

14. A modulator of VDU1 for use in a method of medical treatment.

15. The modulator according to claim 14 which is an antibody against VDU1.

16. The modulator according to claim 14 which is a nucleic acid comprising a sequence encoding VDU1, such that when the modulator is present in a cell VDU1 expression is enhanced.

17. The modulator according to claim 14 which is an antisense RNA comprising a sequence which hybridises to the VDU1 mRNA, a double stranded VDU1 RNA, or a ribozyme which targets VDU1 RNA, or which is a vector encoding said antisense RNA, double stranded RNA or ribozyme, such that when the modulator is present in a cell VDU1 expression is reduced.

18. The modulator according to claim 14, which is a polypeptide having an amino acid sequence corresponding to a portion of the VHL or VDU1 amino acid sequence, and which binds specifically to VHL or VDU1 to prevent VHL and VDU1 from interacting.

19. Use of a modulator of VDU1 for the manufacture of a medicament for the treatment of a condition in which modulation of HIF is of therapeutic value.

20. The use of claim 19, wherein the modulator is a modulator according to any one of claims 15-18.

21. The use according to claim 19 or claim 20 which comprises use of an inhibitor of VDU1 for the manufacture of a medicament for the treatment of a condition in which inhibition of HIF activity is of therapeutic value.

22. The use according to claim 21, wherein the disease is selected from inflammatory disease, cancer, macular degeneration and diabetic retinopathy, Alzheimer's, atherosclerosis, psoriasis, rheumatoid arthritis and endometriosis.

23. The use according to claim 19 or claim 20, which comprises use of an activator of VDU1 for the manufacture of a medicament for treatment of a condition in which activation of HIF is of therapeutic value.

24. The use according to claim 23, wherein the disease is selected from peripheral and coronary artery disease and myocardial ischaemia.

25. A method of treating a disease in which modulation of HIF is of therapeutic value, the method comprising administering to an individual an effective amount of an agent which modulates the activity of VDU1.

26. A composition comprising a modulator of VDU1 and a pharmaceutically acceptable excipient.

27. A composition according to claim 26, wherein the modulator is a modulator according to any one of claims 15 to 18.

28. A method of treating an individual with cylindromatosis by administering to the individual an effective amount of an NF-κB inhibitor.

29. The method of claim 28 wherein said inhibitor is aspirin or prostaglandin A1.

30. Use of an NF-κB inhibitor for the manufacture of a medicament for the treatment of cylindromatosis.

31. Use according to claim 30 wherein said inhibitor is aspirin or prostaglandin A1.

32. A method of treating a disease associated with activation of NF-κB which in an individual comprises administering to an individual an effective amount of an agent which increases expression of CYLD.

33. Use of an agent which increases expression of CYLD for the manufacture of a medicament for the treatment of a disease associated with activation of NF-κB.

34. An assay method which includes the steps of:

providing a cell culture in which CYLD activity is suppressed or missing;

bringing the culture into contact with an agent to be assayed; and

determining the effect of the agent on the activity of NF-κB.

35. The method of claim 34 wherein CYLD activity is suppressed using siRNA.

36. The method of claim 34 or 35 wherein the effect of the agent is determined using a reporter gene construct.